Poster 163

IDWeek, October 21–24, 2026
Washington, DC, USA

Contact: Eri Mizusawa, Shionogi & Co., Ltd
Email: eri.mizusawa@shionogi.co.jp

Bactericidal Activity of Cefiderocol/Xeruborbactam in a Murine Urinary Tract Infection Model

Eri Mizusawa[1], Shinsuke Toba[1], Fumika Takagi[1], Masaaki Izawa[1], Takafumi Hara[1], David C. Griffith[2], Yoshinori Yamano[1]
[1]Shionogi & Co., Ltd., Osaka, Japan, [2]Qpex Biopharma Inc., San Diego, USA

Copies of this poster obtained through Quick Response (QR) Code are for personal use only and may not be reproduced without permission from IDWeek 2026 and the authors of the poster.

BACKGROUND

- Cefiderocol (FDC) is a siderophore-conjugated cephalosporin with potent activity against Gram-negative bacteria including carbapenem-resistant strains. Certain β-lactamases, such as New Delhi metallo-type β-lactamase (NDM), have been shown to contribute to decreased susceptibility to FDC.
- Xeruborbactam (XER) is a novel β-lactamase inhibitor that inhibits serine- and metallo-type β-lactamases. Previous *in vitro* studies[1] demonstrated that XER enhanced potency of FDC against FDC non-susceptible Enterobacterales that produced various serine- and metallo-type β-lactamases.

OBJECTIVE

- To evaluate the contribution of XER to the efficacy of FDC against Enterobacterales isolates with FDC MICs ≥4 μg/mL in a murine urinary tract infection (UTI) model.

MATERIALS AND METHODS

- Four clinical Enterobacterales isolates with FDC MICs ≥4 μg/mL (2 *Escherichia coli* and 2 *Klebsiella pneumoniae*) were used (**Table 1**). The β-lactamase profile for each isolate was determined by PCR or whole-genome sequencing.
- MICs of FDC, either alone or in combination with 4 μg/mL XER, were determined using iron-depleted cation-adjusted Mueller–Hinton broth (ID-CAMHB) according to the 2026 Clinical and Laboratory Standards Institute (CLSI) guidance for FDC susceptibility testing. MICs were also determined using CAMHB, with the endpoint defined as complete inhibition of visible growth, consistent with the FDC/XER susceptibility testing methodology approved by CLSI and EUCAST in 2026.
- Neutropenic ICR female mice were infected by transurethral inoculation of bacterial suspension (10^6 to 10^7 colony-forming unit [CFU]/mouse). Infected mice were dosed subcutaneously with a previously described humanized dosage regimen of FDC 100 mg/kg q2h, with or without XER 20 mg/kg q2h, which was efficacious in a murine thigh infection model,[2] over 24 hours starting at 2 hours after inoculation. Viable bacterial cell counts in the kidneys were measured at 0 and 24 hours after treatment initiation, and changes between pre- and post-treatment were determined.
- Statistical significance was determined using SAS Studio (SAS Institute Inc., Cary, NC, USA).

Table 1. MICs of FDC alone and in combination with XER

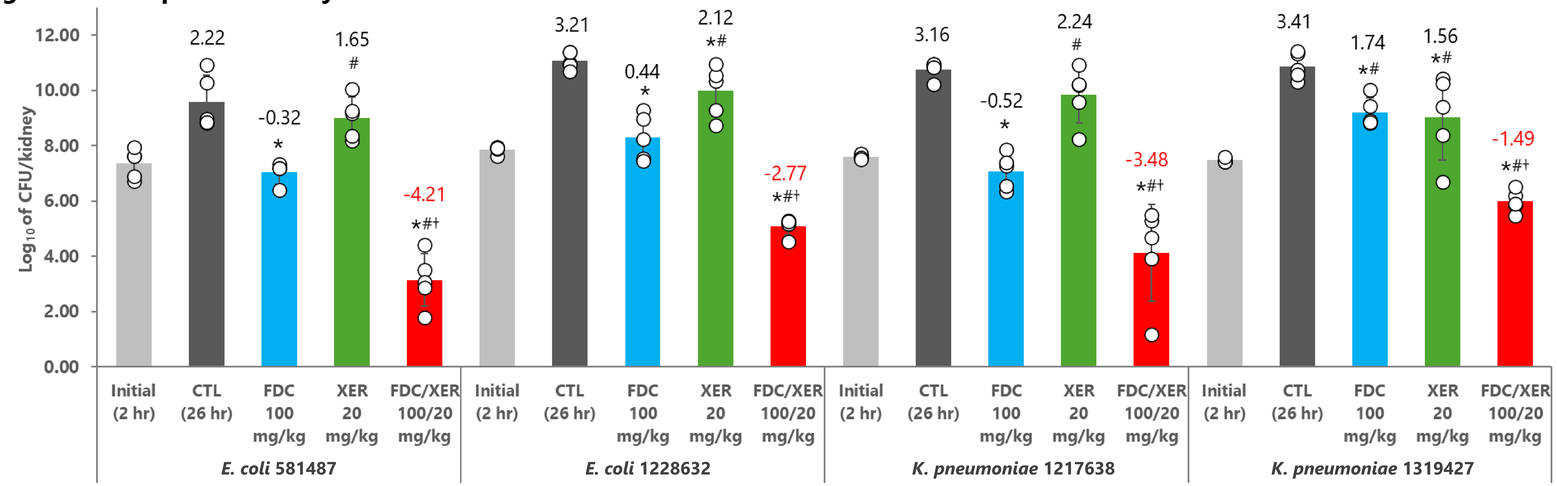
Species	Strain (IHMA No.)	β-lactamases	MIC (μg/mL)			
			FDC		FDC/XER	
			ID-CAMHB[a]	CAMHB[b]	ID-CAMHB[a]	CAMHB[b]
E. coli	581487	EC-15, TEM-1, SHV-12, NDM-1, CMY-59, OXA-9	>32	>32	2	8
E. coli	1228632	TEM-1, SHV-12, EC	8	16	0.25	1
K. pneumoniae	1217638	TEM-1, OXA-9, SHV-12, KPC-2	4	16	1	8
K. pneumoniae	1319427	TEM-1, SHV-1, OXA-427, OXA-9	>32	>32	1	4

[a] MICs of FDC and FDC/XER in ID-CAMHB were read using the significant reduction endpoint.
[b] MICs of FDC and FDC/XER in CAMHB were read at complete inhibition of visible growth (100% inhibition).

Acknowledgments
This project has been funded in whole or in part with Federal funds from the Department of Health and Human Services; Administration for Strategic Preparedness and Response; Center for the Biomedical Advanced Research and Development Authority (BARDA), under OTA number HHSO100201600026C.

References
1. Hara T, et al. Open Forum Infect Dis. 2025;12(Suppl 1):ofae631.1298.
2. Mizusawa E, et al. Open Forum Infect Dis. 2026;13(Suppl 1):ofaf695.1379.

Figure 1. Therapeutic efficacy of FDC alone and in combination with XER in a murine UTI model



Open circles represent individual animal data points. CTL, untreated control group. Data are presented as the mean ± standard deviations (n = 4 or 5 per group). Numbers above the bars indicate the change in bacterial burden from the initial baseline (treatment initiation). Red values indicate >1-$\log_{10}$ reduction from baseline. Statistical significance was determined using SAS Studio. Dunnett's multiple comparison test was used to compare treatment groups with the control group (*P < 0.05) or the initial baseline group (#P < 0.05), and Welch's t test was used to compare the FDC/XER and FDC alone treatment groups (†P < 0.05).

RESULTS

- The addition of XER at 4 μg/mL reduced the MIC of FDC against all isolates, including one NDM-producing strain, when measured in ID-CAMHB or CAMHB (**Table 1**).
- In the murine UTI model, bacterial burdens increased by approximately 2-3 $\log_{10}$ CFU/kidney in control groups across all strains. FDC alone did not achieve a >1-$\log_{10}$ reduction in viable cell counts against any of the strains. XER alone showed no efficacy against any of the strains. Compared with either agent alone, FDC/XER combination showed enhanced activity, resulting in a >1-$\log_{10}$ reduction in viable cell counts for all strains (**Figure 1**).

CONCLUSION

The addition of XER to FDC enhanced bactericidal activity in a murine UTI model against Enterobacterales isolates with FDC MICs ≥4 μg/mL.

Conflict of interest statement
Funding: This research was sponsored by Shionogi & Co., Ltd. and Qpex Biopharma Inc.
Conflict of interest: EM, ST, FT, MI, TH, DG, and YY are employees of Shionogi & Co., Ltd. or Qpex Biopharma Inc.